NEWS RELEASE

BioVie Awarded up to $13.1 Million in Funding from U.S. Department of Defense to Evaluate Bezisterim (NE3107) for the Treatment of Long COVID

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Increasing evidence supports a role for viral persistence, chronic inflammation and immune and metabolic dysregulation in driving long COVID

Bezisterim, an anti-inflammatory and insulin-sensitizer that permeates the blood brain barrier, could represent a novel oral treatment targeting an underlying cause of long COVID symptoms

CARSON CITY, Nev., April 29, 2024 (GLOBE NEWSWIRE) -- BioVie Inc. (NASDAQ: BIVI), ("BioVie" or the "Company"), a clinical-stage company developing innovative drug therapies for the treatment of neurological and neurodegenerative disorders and advanced liver disease, today announced the grant of a clinical trial award of up to $13.1 million from the U.S. Department of Defense (DOD), awarded through the Peer Reviewed Medical Research Program (PRMRP) of the Congressionally Directed Medical Research Programs (CDMRP). The award can provide up to 2 years of non-dilutive funding for a Phase 2b clinical trial that will assess the Company's anti-inflammatory and insulin sensitizer candidate, bezisterim (NE3107), for the treatment of neurological symptoms that are associated with long COVID. The Company anticipates the trial to commence by early 2025.

Long COVID is a condition in which symptoms of COVID-19, the acute respiratory disease caused by the SARS-CoV-2 virus, persist for an extended period of time, generally three months or more. The Centers for Disease Control recently reported that 6.8% of adults in the United States (more than 17 million individuals) currently or previously had long COVID. [1] Symptoms, which include fatigue, cognitive dysfunction and sleep disturbances, are debilitating. The loss in quality of life and earnings and increased medical costs has an enormous economic impact estimated to be 3.7 trillion dollars. [2] To date there are no therapies proven effective for treatment.

Chronic inflammation is one of the main hypotheses that researchers have proposed to explain the persistence of

symptoms in long COVID. [3] Specifically in individuals with "brain fog," sustained systemic inflammation and persistent localized blood-brain-barrier (BBB) dysfunction are key physiological features. [5] Bezisterim permeates the BBB and has been shown to modulate inflammation via the activation of NF-kB, thus representing a novel oral treatment targeting an underlying cause of long COVID symptoms.

"The investigation of bezisterim in long COVID exemplifies the broad potential of therapies targeting inflammation and insulin sensitivity. This approach holds promise for a range of conditions where neuroinflammation is a key player, offering an avenue for advancements in care that are yet to be realized," said Cuong Do, BioVie's President & CEO. "Long COVID symptoms appear to be driven by peripheral and neuroinflammation resulting from persistence of SARS-CoV-2 RNA and spike protein. We believe the accumulating evidence behind this hypothesis supports the investigation of bezisterim to treat symptoms of long COVID and are pleased that this Department of Defense grant will enable further exploration of this molecule's broader potential."

Dr. Michael Peluso, who co-leads one of the first studies to examine the long-term effects of COVID and leads a Long COVID clinical trials program at the University of California, San Francisco stated "I am excited to see the trial with bezisterim receive funding given that recent advances in our understanding of the potential mechanism of action of bezisterim align with emerging evidence for the underlying pathophysiology of Long COVID".

The Preliminary plans for the Phase 2b, randomized (1:1), placebo-controlled, multicenter trial are to evaluate the safety and tolerability of 3 months of treatment with bezisterim, along with its ability to reduce the neurological symptoms that are associated with long COVID, in approximately 200 patients.

Terms of the Award

This project is supported by The Assistant Secretary of Defense for Health Affairs endorsed by the Department of Defense, in the amount of $499,200 for the planning phase with an option to execute the $12,6 million clinical trial after the planning phase has concluded, through the Peer Reviewed Medical Research Program under Award Number (HT9425-24-1-0300).

About Long COVID

Long COVID is a condition in which symptoms of COVID-19, the acute respiratory disease caused by the SARS-CoV-2 virus, persist for an extended period of time, generally three months or more. Common symptoms include lingering loss of smell and taste, hearing loss, extreme fatigue, and "brain fog," though persistent cardiovascular and respiratory problems, muscle weakness, and neurologic issues have also been documented. The Centers for Disease Control recently reported that 6.8% of adults in the United States (more than 17 million individuals) currently or previously have long COVID. [1] The loss in quality of life and earnings and increased medical costs has an enormous economic impact estimated to be $3.7 trillion. [2] To date there are no non-pharmacological or pharmacological therapies proven effective for treatment of long COVID.

Chronic inflammation is one of the main hypotheses that researchers have proposed to explain the persistence of symptoms in long COVID. [3] The expression of proteins associated with inflammation (LGALS9, CCL21, CCL22, TNF, CXCL10 and CD48) and immune regulation (IL1RN and CD22) have been shown to be elevated in individuals with long COVID versus full-recovered individuals. [4] Specifically in individuals with "brain fog," sustained systemic inflammation and persistent localized blood-brain-barrier (BBB) dysfunction are key physiological features. [5] Thus, drugs modulating inflammation, and that work to regulate the BBB integrity, could represent potential therapeutic mechanisms for treating neurological symptoms of long COVID.

About Bezisterim

Bezisterim (NE3107) is an orally bioavailable, BBB-permeable, insulin-sensitizer that is also anti-inflammatory. In addition, it is not immunosuppressive and has a low risk of drug-to-drug interaction. Bezisterim has the potential to reduce symptoms of long COVID, including fatigue and cognitive dysfunction. Persistently circulating viral spike proteins are believed to trigger TLR-4 driven activation of NFkB and the subsequent expression of inflammatory cytokines (IL-6, TNF, IFNg). NE3107 has been shown to modulate the activation of NFkB and thus modulate inflammation.

Bezisterim is being investigated for Alzheimer's disease (AD) and Parkinson's disease (PD). BioVie has conducted and reported efficacy data on its Phase 3 randomized, double-blind, placebo-controlled, parallel-group, multicenter study to evaluate bezisterim in patients who have mild-to-moderate AD (NCT04669028). Results of a Phase 2 investigator-initiated trial (NCT05227820) showing bezisterim-treated patients experienced improved cognition and biomarker levels were presented at the Clinical Trials on Alzheimer's Disease (CTAD) annual conference in December 2022. An estimated six million Americans suffer from AD. A Phase 2 study of bezisterim in PD (NCT05083260) has been completed, and data presented at the AD/PD™ 2023 International Conference on Alzheimer's and Parkinson's Diseases and related neurological disorders in Gothenburg, Sweden in March 2023 showed significant improvements in "morning on" symptoms and clinically meaningful improvement in motor control in patients treated with a combination of bezisterim and levodopa vs. patients treated with levodopa alone, and no drug-related adverse events.

About BioVie Inc.

BioVie Inc. (NASDAQ: BIVI) is a clinical-stage company developing innovative drug therapies for the treatment of neurological and neurodegenerative disorders and advanced liver disease. In neurodegenerative disease, the Company's drug candidate bezisterim inhibits inflammatory activation of ERK and NFkB (e.g., TNF signaling) that leads to neuroinflammation and insulin resistance, but not their homeostatic functions (e.g., insulin signaling and neuron growth and survival). Both are drivers of AD and PD. In liver disease, the Company's Orphan drug candidate BIV201 (continuous infusion terlipressin), with U.S. Food and Drug Administration ("FDA") Fast Track status, is being

evaluated and discussed with guidance received from the FDA regarding the design of Phase 3 clinical testing of BIV201 for the treatment of ascites due to chronic liver cirrhosis. The active agent is approved in the U.S. and in about 40 countries for related complications of advanced liver cirrhosis. For more information, visit www.bioviepharma.com.

Forward-Looking Statements

This press release contains forward-looking statements, which may be identified by words such as "expect," "look forward to," "anticipate" "intend," "plan," "believe," "seek," "estimate," "will," "project" or words of similar meaning. In this press release, forward-looking statements include, but are not limited to, the potential impact of bezisterim on cognition and function among study participants and topline data from the bezisterim trial. Although BioVie Inc. believes such forward-looking statements are based on reasonable assumptions, it can give no assurance that its expectations will be attained. Actual results may vary materially from those expressed or implied by the statements herein due to the Company's ability to successfully raise sufficient capital on reasonable terms or at all, available cash on hand and contractual and statutory limitations that could impair our ability to pay future dividends, our ability to complete our pre-clinical or clinical studies and to obtain approval for our product candidates, our ability to successfully defend potential future litigation, changes in local or national economic conditions as well as various additional risks, many of which are now unknown and generally out of the Company's control, and which are detailed from time to time in reports filed by the Company with the SEC, including quarterly reports on Form 10-Q, reports on Form 8-K and annual reports on Form 10-K. BioVie Inc. does not undertake any duty to update any statements contained herein (including any forward-looking statements), except as required by law.

References

[1] Ford ND, Agedew A, Dalton AF, Singleton J, Perrine CG, Saydah S. Notes from the Field: Long COVID Prevalence Among Adults — United States, 2022. MMWR Morb Mortal Wkly Rep 2024;73:135–136. DOI: **http://dx.doi.org/10.15585/mmwr.mm7306a4** .

[2] Cutler, David M. 2022 The economic costs of Long COVID: An update. **long_covid_update_7-22.pdf (harvard.edu)**

[3] Evans RA, Leavy OC, Richardson M, et al. Clinical characteristics with inflammation profiling of Long-COVID and association with one-year recovery following hospitalisation in the UK: a prospective observational study. The Lancet Respiratory Medicine . 2022;10(8):761-775.

[4] Yin K, Peluso MJ, Luo X, et al. Long COVID manifests with T cell dysregulation, inflammation and an uncoordinated adaptive immune response to SARS-CoV-2. Nature Immunology . 2024;25:218-225.

[5] Greene C, Connoly R, Brennan D, et al. Blood–brain barrier disruption and sustained systemic inflammation in individuals with long COVID-associated cognitive impairment. Nature Neuroscience . 2024;27:421-432.

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